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NATIONAL CHILDREN'S STUDY

VANGUARD CENTERS

PRE-PROPOSAL CONFERENCE

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CASET Associates, Ltd.
10201 Lee Highway, Suite 160
Fairfax, VA 22030
(703) 352-0091

TABLE OF CONTENTS

PROCEEDINGS (9:05 a.m.)

Agenda Item: Welcoming Statement

MS. DESEAU: Thank you for coming today. Yesterday we had a meeting similar to this, talking about the coordinating center. Today of course we'll be focusing on the vanguard centers. The purpose for this meeting is for an exchange of information. It's three fold.

One is we want to improve your understanding of what our requirement is. A second reason is to give us a chance to discover areas that maybe we missed, maybe need to be changed, maybe we should reconsider in the solicitation as it stands. And the third reason, which is an important one is for potential offerors, hopefully those of you in the audience will discover whether or not you're going to be able to meet our requirements.

And the way to discover that is not only in understanding what we are presenting today, as well as what's written in the request for proposal, but also reading the evaluation criteria, because that is the basis on which your proposals will be evaluated.

Right now, since the solicitation has been released, if you want any contact with somebody this project, it has to go through the contracting officer. We are the focal point for all questions, all discussions at this point. Our program office is not able to have discussions with you during this acquisition stage.

The reason for that is that we try in every way possible to make the acquisition fair to everybody. The contracting officer's responsibility is to make sure that everybody gets the same information, and gets it in a timely manner. So, even though you may see people that you know up here on the stage or in the audience, you are not supposed to talk to them, as they are as somebody has said, sequestered during this phase.

You still can talk to them about other things, just nothing about this acquisition. And if they do actually have a conversation, they need to come to us anyhow, to the contracting office.

My name is Virginia DeSeau, and I am the lead contracting officer on this project. There are also Tenishia Alston, and Dawn Rabunsky, names that you will see on the RFPs. They are contracting officers, contracting specialists who are working on the project too. Any of us, plus James Quinn—the names will all be listed at the end of the presentations with contact information. James is the chief contracting officer for our branch, so he is also a source of information.

But again, you can't talk to the program people. And again, the whole reason for that is so that we can make sure that everybody has a fair advantage, and nobody has a greater advantage.

Now, at the conduct of the conference today we are not taking any verbal questions. When you came in, you saw that there were cards. And we are asking that all questions be written, hopefully legibly. And we will go through the presentations this morning, the presentations being Dr. Scheidt will provide an overview of the project, and that will be followed by Dr. Ruth Brenner, who is the project officer for the vanguard centers. She will give you additional information.

Hopefully, during these two presentations, we will have answered questions that you have sent in ahead of time, that others have sent in ahead of time. And maybe just to re-emphasize certain points that are in the request for proposal.

After these two presentations, then we ask you to submit your questions. Hopefully, we will have answered some of them. And the way to do that, there are people who you will see on the periphery here, who have on name tags. They will be runners. If during the presentation you have a question, and you would like somebody to come and get that question soon, you can raise

your hand or hold up your card, and the runners will come and get it.

But during the break after the presentations, if you just submit your cards, they will be evaluated over here. And I say evaluated in the sense that we are triaging the questions so that we are not answering the same one four times. But we are accumulating them, and if it's the same question being asked, we'll just have it answered once, hopefully.

And again, as others come up during the question and answer period, and you want them to be answered, just raise your hand and the runners will come and get your cards, and they will go through this route. So, one question per paper. That helps us in making sure that the questions are distributed to the appropriate respondees.

After the conference we plan to confer and decide what changes we will make in our request for proposal. Now, we are answering as many questions as possible today, and through direct e-mails as they have come in. But what this will result in: changes to the request for proposal, possible changes in the study plan, and possible changes in the statement of work. This is the comment period that we are using right now.

And we want this comment period to only go through December 9. That's an important date for you to remember. It's not a drop dead date. If something comes in, again, we can make further revisions. But our plan is to make as many substantive revisions as possible right after—by the 16th of December, at any rate.

But we want the responses in, the questions, the comments, the suggestions by December 9, so that we have time to consolidate them, and then release the modification by December 16. That will give two months for the preparation of final proposals, which will be sent in. And if there is any problem with those dates, just let me know.

And the parts that you want to be really aware of in the request for proposal are the statement of work, which is obvious enough. That is in Section C of the request for proposal. But also the study plan, which is an attachment in Section J. We are asking that respondents to both the vanguard centers and the coordinating center read the request for proposal for each of the other solicitations.

This project is so intimately tied between the vanguard centers, the future study centers, and the coordinating center that we expect our offerors to understand the roles and responsibilities of both. So, you wouldn't necessarily have to respond to both, but certainly understand who is doing what.

And that is particularly true for these vanguard centers, because the centralization that we are anticipating through the coordinating center actually takes some of the responsibility off of the vanguard centers, such as the ordering of supplies, such as certain communication systems that are set up. Those are all the responsibility of the coordinating center. So, please review at least the statement of work in that solicitation.

And the other thing you want to check is, as I mentioned before, the evaluation criteria. That's in Section M. That should be tied to the statement of work, because those are the factors on which the reviewers will be told to evaluate proposals. The reviewers will be told that they are not supposed to take any prior knowledge of an organization and use that in their considerations, but only what is presented in the proposal. So, be sure that in the development of your proposals you have looked at what the government is expecting for the criteria in the Section M of the solicitation.

The Section L is another really important part of the request for proposal. Section L will tell you how to develop the business proposal, how to develop the technical proposal. There is no tight format for doing so. But it tells you the elements that should be taken into consideration, the

elements that we will be looking for.

So, look at Section L closely, particularly the notes to the offerors. In the development of our statement of work, we have included some—integrated some notes to offerors which we hope will help you when you are putting together a business proposal. But in Section L there is a whole portion that is notes to offerors, and we are hoping that those will be informative to you to have a better understanding of the assumptions that were made in the development of the requirements.

Now, today Dr. Scheidt will give the background of the project, just to review. And Dr. Brenner will give her presentation. Dr. Galke is the project officer of the coordinating center. He also will have a few words to say. And then we'll have a break; and then we'll take questions and answers for the rest of the morning.

Agenda Item: Overview of the Requirements

DR. SCHEIDT: Well, good morning. Welcome to this beginning of the implementation of the National Children's Study. Let me say we've very glad to be here, and to welcome you, and to begin this process of the actual implementation of the study.

We're also very glad to get your input into the science and the details of the study, to try to improve it as much as we can. And we are very glad to offer as much input and help for you to put together the best possible proposals, to make this the best possible project.

I'm going to assume that you are familiar with the documents in the scope of work in the request for proposals, and my comments are not intended to cover any of those details, but to hit just some of the high points for emphasis only. And to anticipate some of the questions that you might have about why this RFP is shaped the way it is.

I'm very sorry that we can't really engage at a personal level. Ginny explained why, and the basis for that. Many of you are friends and colleagues, and we would much prefer to do this with conversations, but for the fairness and openness of this as a public process, it's necessary to go through the steps that Ginny has outlined.

I do want to emphasize that since the questions will be in a written format, I urge that when we answer the questions, if we either haven't answered the questions, or you still need additional detail, please follow-up with additional questions as well. The main purpose of this morning's session is exchange of information, and we want that to be as complete as possible.

In reviewing the background of the study, I am just going to emphasize for emphasis only, where this study came from. And the purpose of these few comments is to emphasize that the proposal for this study did not come from a few feds sitting in a room saying I think this would be a great study. Let's do this.

It came from very high level considerations beginning with the president's task force on environment health risks and safety risks to children. Most of you have heard me talk about this in the past.

I'm not going to go into more detail than simply to say that this task force, charged with the responsibility of developing national strategies to reduce the risks of environment exposures to children, realized the convergence of the vulnerability of children, a great many varied exposures for which there was considerable concern and not information about outcomes, many conditions that children have for which there is reason to suspect environmental contributions, and a number of explicit examples of how this occurs, such as experience with lead and various medications and media, et cetera.

This convergence of factors led the task force to propose a kind of study that could answer these questions. And the task force undertook considerable deliberations and

consultations with studies around the world to confirm that it was reasonable, prudent, and possible to undertake a study that they advised should be bold, and involved all components of government with a stake in it, and the world of academic input, and other stakeholders.

Work then began on this project with the lead agencies that were involved, both with the task force and in beginning to plan this study. And in the fall of 2000, Congress in fact authorized that NICHD proceed with conducting a national longitudinal study of environmental influences on child health and development, reaffirming and defining environment very broadly, and emphasizing the importance of children's health and children's development.

The concepts of the study that have been embraced and used as guides for the planning are listed in these next two slides. And it's these concepts that have led to the RFPs that you are here to consider. And those concepts, as a guide by the planners of this study and especially the interagency coordinating committee, are: that it be a longitudinal study of children and their families and their environment; that it be national in scope; that it be hypothesis-driven; that environment be defined very broadly, including chemical, physical, biological, psychosocial, and cultural factors.

That it be able to study uncommon but burdensome and important conditions of children such as autism, diabetes, cerebral palsy; and those conditions will require for adequate power, a sample in the order of 100,000.

That it concern itself with exposures in the vulnerable periods of early pregnancy, and therefore observations and recruitment and enrollment begin early in pregnancy; that it be able to use the advances of the human genome project and be able to understand how environmental factors interact with genetic expression, and therefore include and collect extensive genetic information, as well as environmental data.

That it include state-of-the-art technology to enable sophisticated techniques for tracking, for measurement, and for the management of really massive data sets; that it be planned and carried out with the involvement and participation of all those federal agencies that have a stake and an interest in children's health and children's environments.

That it also be carried out where applicable, with the use of public/private partnerships; and finally, that in spite of the fact that hypotheses are necessary for guiding and framing the study, that the planners should recognize that the data generated will provide opportunities for answering a great many questions and hypotheses for decades to come, and that data and samples should be collected and stored in ways to optimize this potential. Well, these were the guidelines that we have used in setting out to plan this study.

The process for planning it involved a number of entities. And in considering engaging in this study, as you may be, with contemplation of participating as vanguard centers, it's worth noting what these entities are, and how they fit into the picture of the planning.

The majority of the planning and operational decision-making has been carried out by the interagency coordinating committee, comprised of senior staff and scientists of four agencies that have funded this planning phase: the National Institute of Child Health and Human Development, the National Institute of Environmental Health Sciences, the Centers for Disease Control, and the U.S. Environmental Protection Agency. And that interagency coordinating committee has been largely responsible for operational decisions, and will continue to have that role.

Early on in the process we realized that there was a need for much greater breadth and depth of scientific expertise to plan this study. And in order to gain that, we sought to establish a federally chartered advisory committee under the Federal Advisory Committee Act, and that

advisory committee has been active, and will continue to be active. It provides advice in a wide variety of areas, but advice only.

It is, however, the mechanism by which the considerations of the study can be assured to be a public process. Under the advisory committee have been a number of working groups that were convened in order to provide greater depth of scientific expertise. There were 22 working groups comprised of both federal and non-federal scientists, largely engaged in defining hypotheses and establishing findings on design measures to be used in the study.

These working groups have provided their findings to the advisory committee, and through that, as a public process, the advisory committee has forwarded them to the federal agencies involved. Many of the working groups have largely finished their responsibilities. Some will continue, and the advisory committee will probably continue to use some working groups as needed, as the study goes forward.

But to carry out a project of this scope and complexity requires real work by staff. And in order to do that, a program office has been established at NICHD to do such things as draft and produce requests for proposals, as you have seen recently announced, and a great many other activities.

This program office is responsible for operations of the study, and in that sense, as the study moves forward, will house the project officers who are ultimately the responsible officers for providing guidance to all of the contract entities of the study. From a legal standpoint, the authority comes through the contract office to the various contractors.

It is staffed with: pediatric epidemiologists; environmental epidemiologists; a behavioral scientist; developmental toxicologists; environmental exposure assessment specialists; a statistician; geneticist; and experts in information technology. A number of these are part-time details from various federal agencies, the EPA, and the CDC especially, but when they are working on this they are wearing a program office hat.

These processes that we have used in developing the study include a number of workshops. In fact, they number now 27 workshops, and more are still planned. And the reports from these 27 workshops are on the Web site, and you are invited to use them in the preparation of your proposals. We used them in the preparation of the RFPs.

There have been a number of pilot studies, such as focus groups or testing the feasibility of specific methods, and a number of very complex and detailed scientific reviews. All in all, taking the working groups and all of the participants in these workshops and processes, a total of 2,425 scientists and individuals have participated in this planning process.

Let me talk now just about a few of the major decisions that we have made along the way in developing these proposals that may answer a few questions. I have already mentioned the advisory committee and working groups, and will mention how they interact, and the sampling strategies and how we came to those.

The advisory committee and its working groups, as I alluded to previously, were constituted to participate in the scientific development, and to provide broad and detailed scientific input and consultation. And that has been a very important and highly valued part of this planning process.

In addition, however, involving the number of scientists that we have had, that we have involved in this process has been important for the scientific community and the community of advocates and advocacy groups around the country to gain an awareness and provide support for the study as needed. The advisory committee and its working groups actually included 478 individuals in this planning process.

As we began to engage in developing the RFPs, which include details of the study plan and the scope of work, it became necessary, because we anticipated so many of the individuals participating in this process would be candidates to help in actually carrying out the study, that we had to provide distance between those entities, those academic centers and academicians and investigators, and this planning process.

And for that reason, the advisory committee and its working groups have been at, shall we say, pause for several months. And that pause will continue until past the due date for the proposals that we have solicited.

We do, however, value and will continue to value the advisory committee and its input, and plan to continue very actively, the role of the advisory committee. A new chairman, Dr. Alan Fleischman has been nominated, and the charter for the advisory committee has been forwarded to the director of NIH, and to the secretary of HHS for revision to enable us to make these changes, and to have Dr. Fleischman serve as the chair of the advisory committee.

It will focus on a number of important areas, especially ethical deliberations, a mechanism for thorough consideration of proposals that we should know about from the broad scientific community. It will look at the extent to which we are adequately engaging and including the communities in which the study is being carried out, and other areas of focus as well.

As you know, we have held that hypotheses are important in the planning process for this study, especially to provide the boundaries for the study, and the framework for the planning. Hypotheses are also important to lay out in order to insure that in fact the questions we think should be answered by the study are in fact answerable. And if we don't go through those steps, then we may not be able to provide those answers at the end of the day.

We have also held that for costly elements of the study there should be adequate hypotheses that justify the need for these federal expenditures. Criteria for hypotheses are that they be important for child health and development, that they require a study of this size, that they be measurable with a study of this size and require the follow-up as necessary.

However, we recognize that science evolves. And hypotheses, as guiding framework for the study, will evolve as the science and as the study evolves. So, this is a dynamic process in which we expect to see some hypotheses become outdated, and other hypotheses emerge that had not been considered before and become incorporated into the study.

Why a contract mechanism? A great deal of consideration was given to this decision, and basically the decision was made because of the national scope of this study, and the view that a number of entities, centers, and other entities would be necessary in order to carry out this study, and to assure a consistent, rigorous core protocol was carried out at all sites. A contract mechanism was the best available mechanism to provide that consistency and continuity.

In addition, it was important to assure that the study stayed on the path that it was intended, that a certain measure of control through the contract mechanism is important to assure that the study does in fact address the goals of those agencies that are funding it.

If you look at the scope of the relative control and independence with various funding mechanisms, one has with fairly stringent control, the contract mechanism on one end, with a considerable independence for funding research, the grant mechanism at the other end. And in the middle is what we call a cooperative agreement, where investigators compete for ability to do the work, and then form a team with federal scientists to carry out research more or less as a partnership.

We view that the National Children's Study on that scale of control and independence is

between the strict direction from the federal government of a strict contract, and a partnership of the cooperative agreement. And we highly value and need the input from scientific investigators that we will bring into the study through the mechanisms proposed. And we'll view this as a partnership that will involve input from investigators, as well as the federal agencies.

And this relative position on the scale will vary as circumstances change and as the considerations vary depending on the decisions and the considerations to be considered.

The sampling strategy and the centers strategy—if you notice, I titled this slide, "Sampling and not Versus Center Strategies." An enormous amount of consideration and effort was given to these strategies. Many people considered that a national probability sample—that the decision was either a national probability sample or a center-based implementation sample, and that they were mutually exclusive.

We spent two years, at least nine detailed scientific reviews, several advisory committee meetings, a special workshop of a panel that was convened of national experts, and untold hours of deliberation considering these issues of the sample and its implication on implementation.

The conclusion of this process was that a national probability sample was important, and we would use a national probability sample for two reasons. The first is that the exposure-outcome relationships be representative of the U.S. population, and be generalizable to the U.S. population. And the best way to assure that is a national probability sample. It was not undertaken in order to provide prevalence estimates of conditions or even exposures. But understanding those relationships and the applicability of the relationships between exposure and outcome to the U.S. population was considered to be very important.

The second reason is that important exposures of concern in the study were highly varied. This is not a study of just one type of or one class of exposure. If it was, you could go after that exposure. But the exposures in this study are highly varied, and for many, if not for most, the distribution of those exposures is not known.

And given that we don't know precisely where they are, the best way to not miss them is to do a probability-based sample. For that reason, we accepted the advice of the panel that we convened from the advisory committee, and proposed to implement a national probability sample.

However, we also viewed that centers of excellence are essential to participate and carry out this study as well. We think that because we need the broad scientific input and the excellence in those centers to engage in this study, and we need their expertise. Secondly, a great many of the measures to be performed in this study require center-based expertise and facilities. And we thought it best to use a center-based strategy to carry out the study.

How do you merge those two strategies? Dr. Brenner will describe in much more detail how we chose the sample and how that will be implemented in the study. But this is a unique and challenging combination. Let me emphasize that to do this will require flexibility and adaptation of the centers to the scientific design.

And it's clear that we are asking the community of centers and investigators to come together to carry out this study, the design selected totally on scientific principles, and to adapt to the design that is proposed. We recognize this, and we recognize that for some centers it will be very challenging, and more challenging than others.

Also, this strategy will require support, back-up, and guidance by the coordinating center supporting and working with the study centers in order to successfully carry out the study.

As I have mentioned a number of times already, we consider scientific input from the community of investigators to be extremely valuable, and we will continue to use the advisory

committee to engage the scientific community. We will continue to have workshops as needed, to define the state of science and technology in various areas that are needed.

And through this process of the RFPs, and your response to and input, both at these meetings and in writing, we will continue to gather more input, and modify and improve the design of the study. We expect to gather input from the scientists in the coordinating center, and from the centers carrying out the study, and that input will be part of the scientific process of the study.

We expect to continue to have national and regional meetings to gather additional scientific input, and we invite input on an ongoing basis through the assembly listserv.

There are a number of participating entities in place. We have a scientific support contract that has engaged in carrying out a number of the reviews and providing support to the program office on a variety of scientific tasks as needed.

There is an information technology development contract that is alluded to in the RFPs, especially for the coordinating center. I just want to point out that the prime IT contractor under that contract has excluded itself from competing for the coordinating center so that they can continue to be actively engaged in this process without risk of conflict of interest.

Over the next year, as you know, we intend to go forward with the initial centers. We are calling them vanguard centers. And the clinical and data coordinating centers, and following that the following year and as quickly as possible, will be the establishment of a sample repository and the necessary laboratory services.

The projected timeline for this process—we are now in 2004, having just more or less finalized this set of hypotheses and developed the study design through the study plan. Over the next year we will be selecting the initial centers, and in 2006, complete and pilot the full protocol.

Let me point out that there is an intentional and measured non-specificity in the study plan that is purposely there in order to incorporate the scientific input from the centers and the coordinating center and the processes that I described previously order to finalize the protocol with this subsequent input. And then we expect to enroll the first participants with the initial centers in 2007, and to select the additional centers in 2006 and 2007.

Anticipating the first question that I would expect to get, what's the status of funding? And this slide is a non-answer. And the detail you seek, because of the contracting process, we are not able to provide. What we can say is that projections developed based on pre-RFP assumptions projected the total cost over 25 years of the study to be in the range of $2.7 billion.

Anticipated 2005 funds that are in the president's budget for 2005 allow us to initiate these allowed procurements. And contract regulations are very strict that if we don't have the budgeted funds to do what we are proposing to do, we can't do it.

The professional judgment estimate for the 2005 budget initially was approximately double the funds allocated. And so, we set out these procurements with the intended flexibility to be able to use these funds as well. Contract guidelines, however, do not permit announcing the amount of funds that are specifically budgeted for these contract procurements.

So, those are the high points that I wanted to review with you, and I very much look forward to your questions and your input.

Ginny mentioned that the primary contact for questions specifically about these RFPs is through the contracts office at NICHD, and these are the e-mail addresses and the telephone numbers and the specific individuals. Virginia DeSeau is the contracting officer for both contracts and contract specialists working on the coordinating center; Tenishia Alston, and her

address is provided; and Dawn Rabunsky is the contracting specialist for the vanguard centers. So, with regard with to the vanguard centers, the primary contacts for most of you would be Dawn and Ginny.

In addition, in case you haven't checked the Web site for the National Children's Study, our public Web site is the *nationalchildrensstudy.gov*, and on that Web site you can join the list serve to receive various announcements, if you haven't already, and/or e-mail us directly at the program office.

With that, thank you. And I would like to say do you have any questions, but I can't.

MS. DESEAU: I'd like to make one or two comments while Ruth's presentation gets all ready. One of the comments is that a full transcript of this proceeding, as well as yesterday's, will be available on the National Children's Study Web site. The date that we have been told that it will be available is around December 16, or during that week. It's around the same time as we plan to put out the modification to the request for proposals. And the transcript will also include all of these PowerPoint presentations.

DR. BRENNER: Good morning.

In this brief presentation, I will first present a brief background, just the guidelines that we used in developing the RFP, and more specifically the study plan, and some of the challenges that we faced in developing the study plan, and that we will continue to face as we get into a more detailed protocol.

I'll then turn to the specifics of the study plan, focusing primarily on the sample and sampling plan, because that is where we have been getting the most questions. I'll briefly overview a few other aspects of the study plan, and then turn to the other participating entities, and particularly the coordinating center and the information technology development, and how these relate to the vanguard centers.

We'll then turn to the specific questions. Because we received a number of the questions from multiple offerors, I have included those in the presentation to go ahead and answer them up front. Then we'll take a break, and then go to the questions that you send in today.

So, briefly, and this reiterates a bit of what Peter said, the guidelines that we used were largely taken from the Children's Health Act, and from other advice that we have received since that time. This is a study of environmental influences on children's health and development.

It's a longitudinal cohort study, beginning prior to birth, and continuing through 21 years. The study is national in scope, with a sample size of approximately 100,000 live births. Enrollment is during or before pregnancy, and the environment is broadly defined to include the physical, chemical, biological, and psychosocial.

Some of the challenges that we faced in developing the study plan, and that we will continue to address as we develop the protocol with input from the selected offerors, is that we needed to collect multiple levels of data in a variety of settings including—I haven't listed all of them: environmental specimens collected in the home at multiple time points: prior to pregnancy, during pregnancy, and during childhood; biologic samples, some of which needed to be collected outside of the home and in a clinical setting such as the need to collect specimens at the time of delivery; and a number of measurements in the community such as measurements in schools and in the neighborhoods.

We also needed to capture both intermittent and chronic exposures, and we need to capture these exposures at critical periods of development. It's the link between capturing exposures during critical periods of development, and capturing theseintermittent exposures at these very specific time points that presents a particular challenge. For example, to capture

exposures that occur early in pregnancy, we would have to enroll women prior to pregnancy to get those intermittent exposures that affect that very important developmental period.

Many of these challenges have been addressed in the study plan, and we'll continue to look for innovative ways to address these as we further develop the protocol. And again, all of this is in the context of a national probability sample.

So, with that as background, I will turn to the study plan. So, what is the study plan? It's the document that outlines the general design of the National Children's Study. The purpose of the study plan is to guide offerors so that they are better able to develop their proposals, and begin with a common understanding of the study. It's less detailed than a full study protocol or an operational manual, yet more detailed than many RFPs.

And I want to take a moment, because a number of the questions that we have received have been of the nature of why a particular exposure isn't listed in the study plan, and does this mean that it's not included in the study? And the answer to that is no, that doesn't mean it's not included in the study. The details of specific exposures and outcomes that will be addressed will be specified at a later date, as we develop the protocol. At this point it's a study plan. It's meant to be an outline.

Importantly, the study plan was the first public documentation of many aspects of the study. As I think Peter and Ginny both said, it's currently open for comment. We are interested in receiving your comments. We plan to release a revised version in mid-December.

So, the future documents that aren't yet developed, but will be developed soon are the study protocol, which will be the document developed by the NCS steering committee that specifies data collections for the NCS, and the manual of operating procedures, a document prepared by the National Children's Study coordinating center in collaboration with investigators from the vanguard centers and staff from the program office that will detail all the operational details—basically how we'll do the data collections.

I'm now going to turn to specific aspects of the study plan focusing particularly on the sampling plan, but I just wanted to remind you that I'm not going to go through all the details, because it's in the RFP. It's on pages 43–75.

Well, the sample is a national probability sample, as Peter described the background that went into that decision. Ninety-six study locations were drawn from the full list of counties in the United States, so the sampling frame that we began with was all of the counties in the United States. And I should add that the sample was drawn by the statisticians of the National Center for Health Statistics.

They initially selected the 13 self-representing counties. Those were the counties that were certain to be included in any sample that had this number of counties in it. They then took the remaining counties and placed them into strata based on the factors that you see on the screen: metropolitan status; geography, that's the nine Census regions in the United States; the average number of births per year; and characteristics of the county, including race, ethnicity, and the percent of births that were low birth weight. From these strata they selected the study counties with a probability proportional to the average number of annual births .

And this is the map that you have seen published. There are 21 non-metropolitan locations, 13 certainty locations, and 62 metropolitan, but non-certainty locations. Most of the study locations correspond to a single county. Six of the 96 locations include more than one county due to the small number of anticipated births in these areas.

I'll now turn to selection of the vanguard locations. From the list of 96 locations, that is we started with the 96 study locations that have been selected already, 8 locations were selected

to potentially serve as the vanguard locations. And the way that this was done, again, the 96 locations were again placed into strata. The strata were based on: geography, the four Census regions in the United States; metropolitan status; and the average number of births per year.

And from these strata, two certainty units were selected, four metropolitan but non-certainty units, and two non-metropolitan units. In addition, the sample was drawn such that two locations were located in each of the four U.S. Census regions. And this is the map that was published in the RFP that shows the eight vanguard locations.

I think it's important to note that although there are eight potential vanguard locations listed on the previous map and in the RFP, the number of awards that are made is dependent on the availability of funds and the quality of the proposals received. We anticipate that there will be between 3–8 awards. So, there could be some vanguard locations that don't end up serving as a site for the vanguard phase of the study, and those locations would then be included in the next round of solicitations as a study location, because it's a full sample of 96, and they are all included in the study.

There will be no more than one award for collection of data in a single location. So, we won't have two separate contractors recruiting the same people in a single location.

If there are three awards, our goal is to make one award in one of the three categories, the certainty, non-certainty, and the non-metropolitan. That should be certainty metropolitan, non-certainty metropolitan, and non-metropolitan. This is so that we can learn from the vanguard centers how the study needs to be modified in each of these areas for when we have the full 96 locations on board.

If there are four awards, our goal is to have one vanguard location in each of the four Census regions.

I wanted to mention the mandatory evaluation criteria, because we did get several questions on this, and this is taken right from the RFP. Offerors must be located in the same Census region as the vanguard location. Thus, an offeror's organization must be physically located within the same Census region as the vanguard location for which they propose to serve as a vanguard center.

And I thought it might be more clear if I showed this with another map. This is a map that shows the four Census regions that we used in the study to define this mandatory criteria: the West, the Midwest, Northeast, and South. And within each of those regions are two potential vanguard locations.

An offeror for a vanguard location in a given region must also be located in that region. So, somebody who was in the state of Washington could propose for the site in California, but they wouldn't be eligible to propose for the site in North Carolina.

The reason that we did this was that we anticipate when the full 96 locations are included in the solicitation—again, there is a picture of the full 96—the offerors are likely to be located in some proximity to the locations, because they are so dispersed across the country. And we wanted, as best as we could, to have the vanguard phase give us information that was comparable to what we might see when the full study is implemented.

Within these 96 locations there are 101 primary sampling units. And the importance of this is that the target enrollment is per primary sampling unit, and that's 250 live births per year. So, for some of the locations, for example, Los Angeles, there is more than one primary sampling unit in the study location.

For the vanguard locations, which are the subject of this procurement, each location is one primary sampling unit. So, there is no location where you would need to recruit more than

250 births per year.

I have spoken primarily on the first stage of the selection of the sample, and much less on the second and third stages, the second stage being the selection of segments within the counties, and the third being the selection of households or individuals within the segments. The reason that the second stage of sampling has received much less attention is that for most of the details we're waiting for input from the successful offerors to help us define the segments. But I thought I should at least spend a minute on it.

There are a number of options for defining boundaries of the segments. I think most traditionally Census boundaries are used, but for this study we think it might be more beneficial to use neighborhood boundaries or school catchment areas to help us provide a structure to obtain the community measures that we need.

We will be soliciting input from the successful offerors to help define the segments. But to maintain the integrity of the sample, the offerors will not be involved in the actual selection of segments. And I might add that in some of the non-metropolitan areas, we'll need to target all the births, because there are so few. So, there won't be the second stage of sampling necessarily in all the areas. But for most of the study locations, the number of births are much larger than what we need, and we'll have second and third stages of sampling.

In terms of recruitment of study participants, what is outlined in the RFP is a household recruitment approach. The approach is supplemented with recruitment through other mechanisms such as prenatal care providers. And the reason for doing that is that we anticipate that some groups of women might be underrepresented in the household sampling approach.

For example, a woman who is not planning pregnancy might be less motivated to participate in the study at the time that they are screened, but the enrollment period is four years, and down the line we want to have a mechanism that they can also come into the study, provide them another opportunity to participate in the study.

This is one approach, but it is also in the RFP that offerors can suggest alternative approaches that would meet the goals of the study. So, in addition to describing how the household approach would be accomplished, they can also suggest other creative ways to meet the goals, which are that participants be included in the study as early in pregnancy as possible.

Again, our goal is to have measures prior to conception for 25 percent of the live births that are in the study. They also would have to enroll a sufficiently large population of women such that 250 births are enrolled in each of the enrollment years, and the live births need to be statistically representative of all live births in the targeted vanguard sites.

This is an overview of the proposed schedule of visits. There is an initial screening visit. There are visits during the pre-conception period, and the number of visits during the preconception period vary depending on a woman's probability of becoming pregnant, with those with a higher probability having a greater number of visits. And then at least 15 visits from pregnancy through 20 years of age. These are just the face-to-face visits. There are additional phone contacts, and there may be additional contacts when there is a change of residence and visits to neighborhoods and schools.

There is much more detail on this in the study plan. I just wanted to emphasize here that the proposals should focus on the five-year contract period, which would certainly include the start-up phase, the pre-conception and pregnancy, and follow-up through about three years of age.

The types of data collection again are outlined in much more detail in the study plan. But to just provide an overview, there are questionnaires and interviews, both face-to-face collections

and remote collections of interview data by computer, telephone, mail, some use of diaries, a number of environmental samples and observations, both clinical and behavioral assessments, and a number of biologic samples, and those are all again, outlined in the study plan.

Now, I would like to turn to the participating entities. This is the same slide that you saw in Peter's presentation. The two entities that I think we need to say a few words about, and I have asked if Warren Galke could come and talk about the information technology development and the coordinating center, because those are the two areas where there is the most overlap with the vanguard centers.

DR. GALKE: For those of you who were here yesterday to hear the full blown talk, I won't apologize, but I will acknowledge that I probably won't say the words exactly the same, but the intent is exactly the same. No change has occurred overnight.

The first two slides are going to illustrate some of the key roles that the coordinating center will play in the National Children's Study. Several of them are pretty consistent with most multi-center studies. There are some that are rather unique, and I will highlight some of that as I talk.

One of the unique elements is that there is going to be a requirement for the coordinating center to provide scientific support to the National Children's Study program office for future evolution of the study. As Ruth's presentation indicated, right now we have outlined what's going to happen from before women become pregnant, through the child's third year of age.

We have virtually no more detailed planning beyond the third year of age. So, these scientific support activities will focus to a large degree, on identifying what do we want to collect, why do we want to collect it, how do we want to collect information on toddler, school years, and through adolescence.

The coordinating center will implement and support the information management system. The information management system we consider critical to the overall success of the National Children's Study. A study of the magnitude, the breadth, the scope, the geographic coverage—we are going from Honolulu to Worcester, Massachusetts—we are going to have to rely on the maximum use of computer energy rather than typewriter to successfully complete this study.

The information management system will be developed by our IT contractor, but the coordinating center will maintain and implement it with the vanguard and study centers. And the coordinating center will act as the conduit to feed feedback into the development loop to identify needed changes to maximally make the IMS useful to all of you.

The coordinating center will insure the development of the detailed study documents in conjunction with the National Children's Study program office and the vanguard centers, and then subsequently as those documents evolve when we have the full range of study centers, they will be partners in this process as well.

The coordinating center will be the developer and the implementer of the extensive QA/QC program that we intend to implement in this study. More standardly we will talk about how the coordinating center will develop and implement the study coordination procedures. They will do the routine data management processing. They will be responsible for doing the statistical number crunching for the key critical study hypotheses.

We are committed in the Children's Study to get our answers out to the country as quickly as we can. And you will see when you look at the coordinating center document that that concept is strung throughout our efforts.

The coordinating center will be responsible for providing support to the vanguard centers in the implementation of the multi-stage probability sampling—the definition of the segments, if

we need to do that. They will be working with you to provide guidance and technical assistance in defining the segment boundaries with your input, and then the coordinating center will actually draw the sample from the sampling frames that get developed.

Importantly, the coordinating center will also serve as a study center for children who move out of the areas in which they were initially enrolled. So, they will become in essence, one of you. The other possibility is if a study center or a vanguard center were to fail, the coordinating center will be prepared to step in and perform those functions in that locale.

In terms of the information management system, this graphic just basically re-emphasizes the partnership aspects of this particular implementation plan. The vanguard centers will potentially suggest changes to the IMS based on experience. "This routine for data tracking doesn't work. Or gee, if you only added this one piece of information, my life would be 1,000 percent simpler."

Those suggestions will bubble up and join suggestions being generated by the coordinating center and the IMS contractor themselves. They will be collated and brought to the program office for approval. The program office will be the gatekeeper for changes in the IMS, because the IMS is a principal tool for getting consistency across the 96 study locations, and ultimately between 40 and 50 study centers. So, we want this to be a National Children's Study done in as similar a manner as we can for the core hypotheses.

Another element that I think will impact you in terms of the vanguard activities is that the coordinating center will maintain a 24 hour a day, 7 day a week call center which will be responsible for serving as a communication link between the varying participating entities. You have protocol interpretation questions. You call in on the number, and you will get assistance on getting your questions answered.

They will also serve as a communication link between the study participants and the study, potentially involved with setting up visits and the like, also for study participants to call and say, "I've got a question. Why am I participating in this study? Or that letter that you sent to me two weeks ago, what did it mean?" These kinds of things.

And the other key feature here is that the call center will also serve as a remote data collection source. This is especially true in the pre-conception part of the study, where the call center will be doing telephone monitoring of the eligible women's pregnancy status during the time that we are intensively following the women for their pregnancy.

Thank you.

DR. BRENNER: Thank you.

I was now going to turn to some of the specific questions that we have received, and then after that we'll take a break, and Ginny has a few more comments.

So, the first question we have received from a number of offerors is will additional study locations be added? There is no plan to add additional locations beyond the published list of 96 locations. However, within the already specified 96 locations, there is a possibility that additional adjoining counties may be added. And this particularly applies to those non-metropolitan locations that have a very low number of births annually.

The number of counties that were chosen initially were based on a fairly optimistic recruitment rate. We did join counties to make sure we had a base that was large enough to support the study. But it was based on recruitment rates that we have seen for example in NHANES. And because of the complexity and the duration of this study, we may be adding some additional counties in some of those locations.

Most importantly, this may affect the vanguard location in Minnesota. That's the Yellow

Medicine, Lincoln, and Pipeston— those three counties that are adjoined. We may be adding an additional county. We are actually considering a number of options, and we will be publishing that in the modification to the RFP.

It is very unlikely that it will affect the vanguard location in North Carolina, where the number of births are much greater.

Who can submit a proposal to serve as a vanguard center? I covered that. This is primarily related to the location of the organizations, and I think I covered that on the map, but please don't hesitate to send in another question if that's still not clear. It's any organization in the same Census region, as the vanguard location.

Does the vanguard center have to collect data in the vanguard location? The study participants must reside in the vanguard location. That's outlined in the study plan. But the actual data collection doesn't have to occur in the vanguard location.

So, for example, if there are number of deliveries that occur in an adjoining county, but the residents live in the vanguard location, you could collect data—in fact, you would be expected to collect data- at those hospitals that are in close proximity to the vanguard location.

Are the vanguard centers part of the large NCS? The answer to that is yes. As I outlined, they were chosen from the original 96 locations. In terms of combining the data, the data collected during the overlapping period of enrollment, it is anticipated that that will be combined with data collected at the additional study locations. There is one year that the vanguard locations are currently planned to be enrolling, that the other locations aren't yet enrolling.

So, when we make inferences to the nation, there may be some complications with combining the data that are over different enrollment periods. But for other analyses that aren't making inferences to the nation, the intention is to be able to use the complete data set.

Will participants who reside in the vanguard location, but give birth outside of the vanguard location, be included in the pool of participants to be enrolled? And again, this is a similar question to the last one. Yes, in fact it's important that they are included, and that offerors include those delivery hospitals, and are able to work with those locations.

We have a number of questions related to the adjunct studies, so I thought I would take a minute to talk about the adjunct studies. The adjunct studies are described in multiple places in the RFP. They are in the statement of work.

They are mentioned in the study plan. I think that's probably going to be the most detailed description that you will see. There are a number of notes to the offeror about adjunct studies, and they are mentioned in the evaluation criteria. The adjunct studies are studies that build on the core protocol, but yet add to the core protocol. They contain some additional aspect. They can be performed on all or a portion of the subjects that are enrolled at that center. In the study protocol two types are mentioned, community-focused and center-focused. And again, I refer you to the study plan for that.

We were looking for adjunct studies that effectively utilize and add to the core sample measurements. So, they make use of the structure that is set up through the National Children's Study, but add to that. Importantly, they can be funded through the NCS or through other mechanisms.

We had a number of questions asking about how the adjunct studies will be—how will we decide which ones are done and which ones aren't, we don't go forward with? And the answer to that is that following establishment of the steering committee, a process for evaluating and approving adjunct study proposals will be developed. So, that process has not yet been developed, because we do want the input of the investigators from the selected vanguard centers,

and also from the coordinating center to help develop that process.

This is taken again straight from the study plan, but I just want to remind that award of a contract for an organization to serve as a vanguard center does not constitute approval of the adjunct study, because again, the process for approval of the adjunct studies is yet to be developed.

I think that that answered a number of the questions that came up about adjunct studies, but some of the specific questions were how much detail should be included in the proposals for adjunct studies? Some information is included in the notes to the offeror, which is on page 135. However, we will be including more detailed guidelines on this topic as modification to the RFP.

It is anticipated that certainly we are not expecting to see a proposal for adjunct studies that is equal in detail and in volume for the proposal to serve as a vanguard center. But we will give some more specific guidelines on that. We anticipate about a five-page proposal for the adjunct studies.

What access does a center have to data from the adjunct study? Our intent is that the center conducting the study would have access to the data, however, the details of this are certainly going to vary with the specific design of the particular adjunct study. Some of the adjunct studies may be so linked to the data from the core protocol that we would have to look at those on a case-by-case basis, and again get the input of the data center and the steering committee.

And again, the phone numbers and contact numbers in case you missed them the last time. And that's it.

MS. DESEAU: Before we take a break, a couple of comments that I wanted to give you. You have already met three of the people sitting at the panel. That's Dr. Galke, who is the project officer for the coordinating center; Dr. Scheidt, who is the director of the NCS, National Children's Study; and Dr. Brenner, who will be the project officer for the vanguard centers. Now that you know those people, you can't talk to them.

And on the end there, is Dave Songco. He is our IT expert. So, any questions that come up today about the IMS, the information management system or information technology contractor that is already in place, or how it's all going to blend together, Dave will be able to answer those.

I also wanted to make one more comment. Dr. Scheidt's presentation told you about the over 2,000 people who have participated in the development of this study. Those people, some of them, can come in with proposals. All of them can, actually. Some of them will, some won't.

But I want you to be assured that there is no preference given to these people. Every bit of information that they have has been made public. We have made great efforts to not give them any proprietary information, no advantage over the competition or the competitive status of the project. So, be sure we've done our best to make sure that they don't have any more advantage than those who have not participated in the development and planning stages.

Just again, one of the other points that was made this morning already is about the number of sites that will be selected for the vanguard centers. We say three to eight. That is dependent on funding and the quality of proposals. But in light of our funding environment, we also have built this into the requirement options, which means that we know that we can fund 15 months of this study for sure.

We plan to keep it going forever and ever. But if funding does not come through, the option periods will be evaluated each year on an overall study basis to decide if the study will continue. And that's primarily focused on funding. So, be aware that when you make your

proposal, you have to address it as a full five-year project, as Dr. Brenner has suggested. But be aware that each year after the 15 months is an option period, and that is primarily dependent on our funding environment.

Yesterday, for those of you who were here, and for those who weren't I'll tell you, somebody asked a question about will there be a list of attendees posted. And the answer yesterday was no. But sleep does wonderful things for people, and I got to think about it a little more. And there is really no advantage to us to keep that a secret.

So, the answer to that question today and henceforth is yes, we will post a list of people who have attended yesterday's conference, as well as today's. There is no competitive advantage to being here, because the transcripts and the PowerPoint presentations, all the questions will be made public information. But you can look at the list to see whatever you want to find.

One other point I want to make is Dr. Galke mentioned many specific things about the coordinating center, and one that sticks out in my head that may answer some of your questions too is that one of the roles of the coordinating center will be to schedule the visits. The IMS system is so crucial to this project, and that system will be a centralized source to schedule visits within your sites.

That may have an impact on what level of effort you propose, the kinds of people that you propose, so keep that in mind too. It's in the requirements, but it is important for you to look at that statement of work for the coordinating center, and see each of the responsibilities that they will have.

So, we'll take a break now, and give your questions to the people with the name badges. And when we come back, we'll do questions and answers. And as Dr. Scheidt mentioned, if we are not answering your question, send in another one.

Thank you.

[Brief recess.]

Agenda Item: Government Response to Prospective Offerors' Questions

MS. DESEAU: We've got a lot of good questions, and a lot of them are questions that I will need to answer. But we will go through and hit the technical questions first. And then I will interject along the way.

DR. BRENNER: So, one of the questions we received is does the contractor for a vanguard location need to be located within that geographic location, or within a certain distance? And again, for a vanguard location, the contractor needs to be located within the geographic region that the location is in. There is no specified distance from the specific vanguard location, as long as they are within the region.

Is the NCSCC or the vanguard center responsible for training the staff who will do the in-person data collections? The primary responsibility for the in-person data collections will be the vanguard center, but the coordinating center will be involved in training the trainers. So, to keep the procedures consistent, particularly when we get to the full set of 96 locations, the coordinating center will oversee the training of the trainers. The trainers will then go back and train the staff at the local sites.

Warren, did you want to add anything that?

DR. GALKE: The initial training for all study personnel will be done by the coordinating center. The training will be refresher training and training for new hires who fall out of a routine retraining cycle— this is the best definition we have right now.

This is certainly an area where the definition of the study protocol and the detailed operating manuals will better define the precise relationships, but that's basically our concept at

the present time, that we will have an initial wave of training for the vanguard centers, and then for the full study centers. conducted by trainers associated with the coordinating center.

But because of the multiplying effect of personnel training needs when you are talking 40 or 50 operational sites, we'll need a local capability to catch up with the evolution of manpower at the local centers.

DR. BRENNER: The RFP for vanguard centers discusses the possibility that in the eventual study two to three counties may come together in a single proposal. Is there any problem with more than three counties submitting a single application? For example, could a statewide coalition contractor work in all counties in a state or in a region?

And the answer to that is yes, certainly they could. Just to be clear, there are the vanguard locations. Those are the places where the data collections are occurring. And then there are also the centers that are doing the data collection. And one center or centers can come together in a single proposal. In the next phase we anticipate that Centers will collect data in multiple counties, and encourage collaborations.

In other words, we are not anticipating having 96 separate centers when the whole study is in the field. We are anticipating that centers will have more than one study location at which they are collecting data.

MS. DESEAU: I just want to add to that there is a question here about—there are two questions actually that are very similar. One is after the initial phase if three vanguard centers are funded, will the five not funded be preferentially funded in the next round? And then next question is will the vanguard sites be given preference for additional counties later?

The answer to both of those questions is that each acquisition will be independent and selectively competitive. No, there will be no preference for people who send in proposals this time but don't get funded. And no, there will be no preference for adding additional counties at a later date.

When the next solicitation comes out, people would have to respond again. We would assume that after going through the first round, you will already have a system in place for it. But no, each acquisition is individual, unique, and there are no preferences given just because somebody is in a selected location at this time.

DR. GALKE: Can we contact the program office for general discussion about other projects of similar nature, or is this program office exclusively dedicated to this project?

The simple answer is that the program office of the National Children's Study is primarily focused on the National Children's Study. Individual members of the program office may have other responsibilities that they brought with them that represent access or knowledge about other studies, but generally speaking the activities of the National Children's Study program office is the National Children's Study.

MS. DESEAU: So, the answer to that question, which I have fielded to Warren is you shouldn't contact them, not at this stage of the game. Later on after the acquisition is done, you can. But just know they are still your friends. They just can't talk to you right now.

DR. SCHEIDT: The question I have is, the initial authorization for the study extends through 2005. Do you expect a renewal of the authorization legislation next year? Is the legislative proposal to achieve this in preparation at this time?

The Children's Health Act of 2000 instructed us to plan and implement a study, and to report back to Congress over a period of time. We have done that. But we interpret that this does not require repeating authorization. If we were told out to carry out a study that lasts 21 years, that's what we are responding to. And so, we anticipate that this mandate will continue into the

future.

We are not involved in developing any legislative proposals, because we can't do that. We can't do that, and we don't do that. You may want to ask organizations that are involved in this kind of effort what's going on, but that's not something that as federal officials, we organize and orchestrate.

MS. DESEAU: I'll take a few, because I have quite a stack here. A question is, to be considered for a vanguard center must the PI have a history of being awarded a federal grant contract or cooperative agreement? The answer is that no is the easy answer. But there is always this part; look at the technical evaluation criteria and see that there is a past performance evaluation in there. That past performance evaluation is usually based on some federally governed, federally funded program.

So, as long as there is a demonstration of knowledge, expertise, skills, that will be the primary criteria. The technical and personnel qualifications are scored evaluation criteria. But past performance is also a non-scored evaluation criteria. So, we will be looking at all of that in these considerations.

Another one is did any contractor assist the government in study design and selection of the primary sampling units, counties? No, we have had all federal participants in making these decisions. Dr. Brenner already mentioned that the National Center for Health Statistics was a major component in the selection of these sites. So, there was no paid contractor who assisted in that effort.

Here is a big one. Can Booz Allen be a subcontractor for the coordinating center or the vanguard sites? Booz Allen, we haven't announced it today, but a question had occurred yesterday, was asked yesterday of who is the current IT contractor, and that is Booz Allen Hamilton. That's easily obtained public information.

And they have agreed that they would not come in as a competitor for the prime contracts for either of these solicitations. And yes, they can be approached as a subcontractor. Anybody can go to them and request their participation as a subcontracting organization.

Are there subcontracting opportunities in the IMS component with the current IT prime contractor? If so, how do we find out about those, and who should we contact?

Subcontracting opportunities are arranged through the prime contractor. There are flow down clauses, so the requirements for use of small businesses, et cetera, are also from the prime contract, which Booz Allen has flow down from the government. So, what that means is that they go out and solicit and find their own subcontractors. It's done in a competitive way, but we don't have control, we being the government does not have control over exactly how they do that. They find their own subcontractors. We can't point you in a direction specifically.

They can use the same Small Business Administration Web site that anybody uses. That Web site, which I didn't announce today, it is included in the RFP for the coordinating center on pages 105 and 106. That Web site includes small businesses with specified capabilities. And we assume that our prime contractors go to that Web site, as well as knowledge within the field, and people that they have worked with in the past, people that they have learned about from others in the field.

So, I can't specifically answer that. If that's not an adequate answer, you can ask the question again, maybe in a different way if I didn't understand it completely.

I have a whole series of questions about specific costs. So, maybe we'll go back to the technical thing, and then I'll hit these cost questions.

DR. SCHEIDT: Actually, speaking about costs and funding, I have two to address. I

don't understand Peter Scheidt's third bullet on funding. That of professional judgment was two times what?

There is a certain amount of funds in the president's budget for 2005, as there had been for 2004 and 2003; 2005 was the first year that we reached the point that with implementation to advance the study on its projected path, we would need and use additional funds to meet the timeline as optimum. And so, this 2005 year was the first year that we could hope to see appropriations from Congress.

We went forward with these RFPs before the appropriation from Congress. As you know, we were on a continuing resolution until last week I think it was. And that amount that we had indicated would be optimum for us with implementation of the study was double, slightly more than double, what had been in the president's budget, which was the second bullet. And again, the contracting process precludes me from giving you the specific amounts, but those are the relationships.

The second question is will biological samples that are collected be kept even if further funding at some point is not received? And we obviously have not made that decision, and I think the decision would rest on the value of those biological samples for research, and for answering scientific questions at that point.

NICHD does already have a repository contract that several studies have stored data, one of which are the old samples from the collaborative perinatal project. And if these samples would be meritorious for ongoing, continuous research, NICHD and perhaps other federal agencies may well be interested in preserving them, even in the instance of non-continuation of the National Children's Study.

But that is a question that could only be answered at the time, depending on the nature of the samples, the number of them, and the capability of the government. So, that's as far as I could go with that.

DR. BRENNER: I tried to put all the questions related to the sample together, so I can answer these in a more efficient way. So, I'll go through these first, and then try to provide answers. And I'm going to actually ask Randy Curtin from NCHS to answer one of these questions.

Will the study over-enroll so that 100,000 participants remain at completion of the study? Or will the study enroll only 100,000 total? And the answer is neither of those two. The study will enroll sufficient women so that there are 100,000 births, but we recognize that there won't be 100,000 children at age 18 or 20 or even age 3. But the goal is to have 100,000 births, which means enrolling more than 100,000 women.

The RFP says 250 live births per year for five years. Is this a total N of 1,000, or 1,250 at the vanguard centers? At the vanguard centers it's 1,250, because it's a five-year enrollment period, and we know that's a little different than the remaining study centers where we expect a four-year enrollment period. That's because we have the one year of additional enrollment when the vanguards are in the field before the other study locations.

Again, our hope is that the procedures and protocol will be such that we can combine the data, for at least for most of the analyses. . But when we are making inferences to the nation, there is a possibility that only the four years will be used for those specific analyses.

Is it possible for an offeror to suggest substituting a chosen study location, one of the 96, for one of the chosen vanguard locations, or are the vanguard locations set? And the answer to that is the vanguard locations are set. It's the eight that have been announced in the procurement. We are not accepting proposals to substitute another location.

DR. SCHEIDT: Let me expand on that a little bit. The reason for the selection of the vanguard locations, the way we did it was to try to take a sample that would represent the distribution and the problems we would have to solve as much as possible. It wouldn't help us to pull a sample with the top, most excellent and easiest to do places, and then learn erroneously that it was easy to do things when the breadth and variety of sites in the entire sample was more difficult.

And so, we felt that the pulling the vanguard sample in a probabilistic way, the way the entire sample was pooled, and learning from the initial sites what we would have to learn in order to be able carry out this study with the range of types of sites, was critical and that's why we feel it's important to use the approach that we have used with the vanguards as well.

MS. DESEAU: Dr. Fleischman has a couple of questions that he is best served to answer. So, this is Dr. Alan Fleischman. He is the chair of the advisory committee, current chair.

DR. FLEISCHMAN: And ethics advisor to the study, interested in the human subjects aspect of the study.

The first question is when patients are consented to be enrolled in the NCS, are they consented for the scope of work in this technical proposal, or for the scope of work in the full 21 years?

It would be my opinion that any IRB would require that we at least inform potential subjects of our intention to study them in their children throughout the duration of the study. So, we would need at least to give them some information. We hope in the National Children's Study to be innovative and creative in our approaches toward informing and obtaining permission of our subjects.

We believe in continual informing as a process for keeping people involved in the study. I would strongly recommend to you that you not develop consent forms at this time as part of this process, since you do not yet have the final protocol developed, but only the template or study plan.

And that you work with your IRB office to get what might be called an umbrella approval for submission, with the idea that before any subjects are going to be enrolled, you will come back with more specific protocol, and more specific process. We will spend the next year and then working with the vanguard centers to develop the informed consent process. So, there is going to be a lot of work done in that direction between now and when we first enroll a subject.

The second question is will the vanguard centers need to get IRB approval from every institution involved, like delivery hospitals, pediatric hospitals, schools, day cares, et cetera?

It is our hope that the vanguard centers and the study sites will be able to work in a consortia relationship with these kinds of entities, realizing that the federal regulations allow several things. First, the federal regulations allow individual centers to cede responsibility for IRB approve to core perhaps vanguard centers.

It also allows us to develop a centralized process for IRB review. Now, each individual institution will decide whether it wishes to participate in a centralized review, but within your own vanguard site it will be important for you to develop the consortia relationships. And it may be less important on the IRB than it is on the HIPAA side.

So, you have to concern yourselves about obtaining the information within each of these delivery sites, fulfilling the rules of those sites in terms of sharing health information, and getting the appropriate consents. And sometimes the HIPAA consents and the IRB or research consent is different, sometimes it's fused. There are no regulations that force it to go in one direction or another. So, those are institutionally unique problems.

Our hope is that vanguard centers and other study sites will be creative and appropriate in developing consortia, so that they will be able to accomplish this complex goal.

DR. SCHEIDT: Let me answer another question that is related to that. For counties without academic medical centers what do you estimate is the probability that it will be possible to collect cord bloods, placentas, seven days a week, 24 hours a day, and to perform bio studies on newborns before they are discharged from the hospital?

The ability to carry out these in a variety of non-academic centers, as well as academic centers will depend on a variety of approaches and relationships. And we have discussed in considerable detail, the kinds of approaches that might be used. In fact, we visited community hospitals in the Washington metropolitan area to walk through what kinds of procedures and challenges we would encounter with this.

And it could range from establishing new relationships with centers, to having an on-call person available for a region to go to study sites to carry out these procedures. And we are very interested in the centers proposing—looking at creative ways to do this, not accepting that well, if it's outside of a medical center, we can't do it. We think that these are the kind of creative and flexible challenges that we are asking all of the centers to give thought to and propose creative ways to address these problems.

Since this is also related, let's see what it says. Please describe the nature and the level of collaboration expected between vanguard centers and other institutions such as local health departments, hospitals, clinics, et cetera. The previous answer certainly suggested the need for relationships with community hospitals and other entities. We expect the extensive use of partnerships and relationships in order to carry out this study.

That actually relates to the initiative that Dr. Zerhouni has with his Roadmap at NIH. He is very intent on the bringing communities and clinical entities outside of academic medical centers into the research enterprise of this country. That's part of his Roadmap. He has commented about this component of this study as important for advancing his Roadmap. And the challenge to academic medical centers is to forge these relationships and help to make it happen.

DR. GALKE: I'm going to follow up on Pete's answer with a reference to an element in the coordinating center statement of work. And that refers to the scientific outreach program plan where we identify needed activities for using the information generated by the NCS, and providing information back not only to the scientific community, but also to the practitioner community both locally and nationally.

And that is further reinforcing the fact that we intend this study to be different in many ways. And that the level of investment requires us to maximally distribute information. And so, the relationships that you develop in the beginning, in the proposal stage, and then carry through the implementation, think of the whole process as an infinite set of feedback loops where information and technology and other elements are sent back and forth.

DR. BRENNER: Okay, three more questions related to the sample. What is a certainty county? Are the 13 a subset of the 96, or selected outside of the 96? Please give more detail regarding the relationship between the vanguard locations and subsequent locations. Within each vanguard location how diverse is the sampling expected to be? For instance should sampling be representative of urban, suburban, rural populations? Should sampling target occupations at risk such as solvent workers, metal workers, et cetera?

I'm going to answer a couple of these questions, and then ask Randy to answer a couple of them. The relationship between the vanguard locations and the full list of study locations and the certainty locations: the 96 includes all of those. The certainty locations, the 13 are part of the

96.

In terms of the relationship between the vanguard locations and the future locations, again, they are all part of the sample of 96 locations. I guess that I'm not quite sure what question—I may have already answered this question, but if it relates to the protocol, we expect that certain aspects of the protocol will be developed and tried first in the vanguard locations.

But that ultimately there will be a common protocol. It will be refined and then there will be a common protocol that will be used in all of the study locations, including the vanguard locations. And that is why they have that one extra year of enrollment, and then another four years of overlapping enrollment. So, they are a part of the entire study. They are a part of the sample. I guess you can send in another question if you need further clarification.

Then I was going to ask Randy to address the issues of what a certainty county is, and also some of the issues about our ability to perhaps oversample certain populations in the second stage of sampling.

DR. CURTIN: The study design is based upon combining four years of national natality data. So, there are approximately 16 million births in a four-year period. To get a sample size of 100,000 with 100 PSUs and 1,000 for PSUs, that basically sets your stratum size at approximately 160,000 births per stratum size. So, when you put counties together, you are going to be putting them together to form units of approximately 160,000 births per combined stratum counties.

That then leads to the certainty measure of size of 160,000. So, for example, if one county has greater than 160,000 births in it, it is going to be selected with certainty into the sample. Now, it's also somewhat problematic if you are at 99 percent of that, you're not quite at 100 percent of that certainty strata. So, typically in survey design some proportion of that 160,000 is used. For this particular design the measure of size was 120,000.

So, if there were 120,000 resident births in the four-year periods, that county was selected with probability of going into the sample. That left I guess really 12 areas. But we also had this configuration of wanting to have nine Census divisions, so we had to add an extra certainty strata. So, one of the certainty strata actually has far fewer than 120,000, but it was to balance out the regional nature of the sample. So, that's how the 13 locations were selected with certainty.

Other large metropolitan areas which weren't quite certainty were grouped with other large metropolitan areas. So, for example, if you had 40,000 births, and you combined 4 counties each of 40,000 births, then any particular county was selected with probability one-fourth out of that strata of size four.

When you got down into the smaller counties in the non-metropolitans, you might have a 100 or even 200 counties that get together to form a strata. And their probability selection is then based upon the number of births relative to the stratum size.

The other question has to do with the within PSU sampling strategy at the second stage. What will be done is there will be some close collaboration with the program office, with the coordinating center on how to design that. We have a concept for a national design, which is not only to select 100,000 births, but to perhaps oversample so we can look at racial and ethnic disparities.

So, some of the strata that were set up were based upon proportion of American Indians, proportion of Asians, proportion of Hispanics, proportion of Blacks. So, if a county was in a strata that was basically a high density for one of these demographic subdomains, that allows the center that is dealing with that to oversample for the demographic group.

The statistical power to test differences is based upon the smaller sample size. So, we are

going to want to oversample Blacks, Mexican Americans, Hispanics, Asians, American Indians to the extent possible. So, when it comes time to decide how to do the within PSU sampling strategy, you have to look at the sample yield, how it reflects upon the national design for oversampling, what local area information you have available to you in terms of how to form and select segments.

And it doesn't behoove me to tell you exactly how to do that. We want to see what you are putting together in your proposals. But it will have to be integrated at a national level so that we keep the national design intact as well.

DR. SCHEIDT: Thank you, Randy.

The next question, how many study locations do you think will be funded in 2006–2007 timeframe? How many total study locations for the 96 counties are anticipated?

I assume this means study centers, and for the funding 2006-2007, we can't know that. And our aim is to implement the entire study, and we anticipate, based on the instructions we have had from Congress and from the NIH and the lead agencies, that we should proceed with these RFPs, and proceed to implement the study. That's just something we can't know right now.

How many total centers for the 96 counties? As we said in the RFP, we anticipate 30-50, in that range. And that will depend on what we both learn with the vanguard centers and on funding. And that magnitude of the number of centers is based on experience with other large studies of this size, such as the women's health initiative, which had 40 centers for a sample size of about 120. And it's based on estimates of what load that centers can carry, and we'll refine that as we learn from the vanguard experience and funding.

You will need much more money to be allocated by Congress than as in the current authorization. Do you have a campaign of the NCS in Congress?

I can say that as I said before, as federal officials we don't do that. We don't organize and orchestrate campaigns to fund our programs. We respond to both instructions from the administration, and instructions from Congress to implement these programs. We are aware of advocates for the study actively advocating for this funding, and that's as much as I can say about that.

MS. DESEAU: Let me just change direction. One of the questions is what will the location of the coordinating center be? And is there a preferred location?

The coordinating center solicitation is full and open competition. And the award of it will be based on the quality and the best buy to the government. So, we don't know where it will be––anyplace across the United States.

DR. GALKE: Can we operate a local call center and tracking procedures?

This again is in an area where there will be negotiation and fine tuning as the details of the study protocol, as well as the study operating manual, are fully developed. Our intent at the present time is to have a large majority of the workload associated with direct phone collection of data from study subjects being done by the coordinating centers call in center. It will also be the place where there will be an 800 number for study participants.

It is quite conceivable that especially for some of the more rural segments of the population, that a local call center and specialized local tracking procedures may be necessary to do the job. The coordinating center is going to be responsible for tracking our study subjects once they leave their home base. We intend that certainly to be across the 50 states, and we hope, but we're not as confident, that this might also involve if they move out of the country.

But our full hope is that our tracking procedures, both at the coordinating center, and through the local will allow us to trace and keep in contact with all study participants for as long

as we can. We are not dropping, intentionally, anybody based on where they have moved to.

DR. SCHEIDT: Another question, will co-investigators at a study location be able to play a role at the national level? For example, attend the steering committee meetings?

The notion that the steering committee is the entity with primary deliberation of scientific and protocol issues is correct. And we think that's an important entity. We think it would consist of the PIs, as well as representation from the interagency coordinating committee and the program office.

I interpret this question as will other members of the team from a center also participate or be able to attend? And the answer to that is that we are interested in the best science and the best decision-making that we can make. Resources are finite. And what that process consists of and exactly who can attend would be a matter for the steering committee and the program office and available resources.

And so I think I can't at this point say only the PIs would participate. There could be good reasons in cases for other members of the team to participate. And these are issues that the steering committee itself is going to have to deal with in the light of available resources.

Another one, what's the status of the human genome project interest in joining the NCS?

I think some of you may be aware that there is a proposed longitudinal study that the Human Genome Institute is leading now called the AGES Study, which proposes a large cohort followed over 15 years to focus on genetic and adult diseases particularly.

They are much less farther along than the NCS. We are in regular communication with them, and they are a member of the federal consortium of the NCS, and members of our staff participate on their planning process. There has been discussion in their early planning phase of including those participants in the NCS in that age group in their cohort. And that certainly makes sense, and we would agree with this.

The size of the study would have a number of additional—more centers than we are proposing in this study. And so, it would involve these centers and others as well. It's just too early to say the details of overlap, but we are certainly working with them, and we expect there to be some overlap in these two projects if that study is actually implemented.

DR. BRENNER: I have a number of questions related to the number of births per year that need to be enrolled in the vanguard locations. So, I'm still unclear what the expectation of total births in the first five years is. In several places throughout the RFP reference is made to the fact that the vanguard centers will be expected to enroll and follow sufficient women to insure 250 births per year over a five-year recruitment period. However, enrollment is not planned to begin until 15 months or so into the process. Can you please clarify the exact number of enrollments expected during the period of 9/30/05 to 9/29/10?

If an offeror is from a county with a high number of births what sample size should be proposed in the application? Minimum 250 births per year times 5 years, which is equal to 1,250. If 40 centers are eventually funded for 100,000 births, then there will be approximately 3,300 subjects assuming equal numbers.

So, just to try to clarify all of these, as it is stated multiple places, sufficient women should be enrolled to insure 250 births per year, and at the vanguard centers it's a five-year period, so a total of 1,250 live births. The number of women enrolled will be more.

In terms of the specific time period that the births will occur in, there is at least a 15 month start-up period. Fifteen months is what is currently planned. Then there will be time where we will be enrolling women, but there won't be births yet. And so, I think the specifics of when the live births will occur, and the specifics of the enrollment period are actually going to be

detailed in the protocol. But it certainly won't be in the initial 15 months. So, the goal again, is to enroll from the vanguard centers, 1,250 live births in the study. But it means more than 1,250 women.

DR. SCHEIDT: I have a quick one. What plans are there for the coordinating center, vanguard centers, or study centers to handle genetic information that would be generated?

The genetic samples are included the study plan, intended to be included in the study plan. The genetic information, how that would be handled as separate from the remaining data, it would certainly be handed the way the rest of the data will be handled, with the extra concerns about the ethical considerations of how we deal with genetic information.

And Alan, perhaps you could add some additional thoughts about that.

DR. FLEISCHMAN: Specifically related to the genetic information, it is our intention to not reveal that information to the subjects. If in the future there are known specific findings, we expect to inform the public about those findings. And if people wish to have genetic information revealed about themselves, they will seek that out through a clinical arm.

Our genetic data will not be clinically relevant to the subjects as collected. We are though, committed to informing individuals about any clinically relevant information that is found in a timely basis. So that there will be some laboratory tests of biologic samples that are clinically relevant. We are committed to doing those in a timely manner and informing people in a routine manner, or in an emergent manner if needed.

There is one other question that I have been asked to comment on. I may as well do that at this point, because it relates. This is the question. Gaining cooperation to collect environmental samples in schools and workplaces may be affected by the confidentiality of results. Some locations may want results, others may not. How should this be addressed?

Let me first comment on individual subjects and confidentiality. We are fully committed to maintaining the confidential nature of the National Children's Study on the individual subject level. And we will be appropriately applying for all safeguards to maintain confidentiality, and will assume that our IMS systems and every other part of the training of individuals and your work will maintain the individual confidentiality of subjects. Yet, we will give subjects information that is of relevance to them on an individual basis.

In terms of information to communities or information to individual places such as schools or workplaces, here there is a different concern. It may well be in their interest to learn about information, and we will in fact be thinking this through as we begin to develop the data.

The federal advisory committee will have a subcommittee called an ethics advisory subcommittee, which will make recommendations to the steering committee and the program office about how to deal with those specific questions. However, if we find something of clinical relevance in a site, of clinical relevance to those people in that site like students or workers, then we may well have an ethical obligation to inform the site, and perhaps even others if there are legal obligations about those findings.

So, we are quite anxious to fulfill our legal obligations, to be thoughtful about our moral obligations, and we have in place mechanisms to consider those as we begin to develop the data. That may have been confusing, and you may want to ask more questions.

DR. BRENNER: Another question about the number of births per study location. Is each study location supposed to enroll 250 live births per year by a study center? A study center can enroll more than 250 by enrolling 250 per study location, and using more than one study location, correct?

The answer to that is the number of live births targeted is based on the primary sampling

units. In the vanguard phase it's 250 live births per year per primary sampling unit. In the vanguard phase, which is what this solicitation is, each study location contains one PSU. So, it's 250 live births per year over the five-year period of enrollment.

Also in the vanguard phase, there is only one study center per study location. So, the only procurement that is out right now that is for study centers is for the vanguard phase, and it's 250 live births per year over the five-year enrollment period.

When we move to the next set of procurements for study centers, that's when there will be the opportunity to combine multiple study locations in a single proposal. That's also the time when some of the locations contain more than one primary sampling unit. And in those areas, there will be a requirement to enroll more than 250 live births per year, and it's dependent on the number of primary sampling units in those locations. But for right now, which is the only procurement that's out, it's 250 live births per year over the five-year enrollment period.

DR. SCHEIDT: While Ruth is looking at that, I want to make it absolutely clear that we are talking about more than double the number of sites than centers, which means that each center on the average is going to have to have two or more sites. The reason we did that was to get representation. If we had only 30 or 40 sites in the country, the representativeness would be much, much less, and there would be less areas of the country involved in the study.

MS. DESEAU: While Ruth is thinking, I'll pick up a couple of these. Let me give you a general review. There have been a few questions about the review process, who will make up the review panel, who will evaluate the proposals. The standard mechanism for NIH evaluation of contracts is through a peer reviewed system, very similar to that for the grants, but we don't have standing study groups. These are ad hoc chosen reviewers.

So, we will use our Division of Scientific Review, who will choose people with expertise in areas that are relevant to each proposal, the coordinating center and the vanguard centers for instance, perhaps pediatricians, statisticians, even IT specialists for the coordinating center. There will be a group of people who will be asked to participate.

And this is all through our Division of Scientific Review. It's a completely separate department within the NICHD. And the program office can give some suggestions of people that they know who have certain expertise, but the Division of Scientific Review will choose these people. And it will be a broad scope of expertise.

And so, we can't tell you exactly who will be chosen. We can tell you that it will be a nationwide search per se, that the Division of Scientific Review will go to experts in the different fields and see who agrees to participate.

This selection will not be made until after proposals are received, because we want to avoid any conflicts of interest, any potential that the Division of Scientific Review will even suggest to a person whose organization or related organization might be sending in a proposal. And so, you can be guaranteed that the reviewers will not be from any competitor's organization if a proposal is received from a competing organization.

There is one other question. Who is the IT contractor? That has already been answered. That would be Booz Allen Hamilton. And how were they chosen? They were chosen under a similar system. It was a full and open competition. There was an evaluation panel of peers, experts in the field. And that selection was made about a year and a half ago. It might be two years already. But they have been in place for a couple of years already.

Now, that particular contract was awarded by GovWorks, which is not a division of the NIH. But they are the ones who are handling the contract for us.

And another question that has come up is also perhaps related to scientific review, and

I'm not sure if I have answered this question with my previous response. Could you please name the contractor that provides scientific review support? Is the contractor eligible to bid on the contracts for the vanguard centers?

I'm thinking that's not—scientific review support is not exactly what you meant in terms of what I was just discussing. I'm guessing that it ties in with a couple of other questions that are scientific support. Within the coordinating center there is a requirement that scientific support will be a responsibility of the coordinating center.

That is, there is a current contractor, and since again it's public information, Battelle is the contractor we have been using for the past couple of years, who have been producing the white papers, who have been searching out scientific investigations that have been needed for the development in the planning process for this study.

They will be eligible to compete for this project, because every bit of work that they have done has been publicized. There is nothing that is secret or preferential, except that they are an incumbent, which is the nature of the beast. But there is no preferential treatment towards their organization, and everything that they have produced for us is available either on the NCS Web page or has been taken into consideration in the writing of the RFP and been made public in that way.

DR. SCHEIDT: I have two questions about community participation. Would you clarify the role of communities in the study, especially since this is not a pure community-based participatory research endeavor? Correct.

How should vanguard sites balance the need for sampling within a county in a way that is statistically representative with utilizing community-based opportunity to access participants?

The selection of the segments within a location is to be carried out in a probablistic way, as the entire national sample was carried out. So, that it's not possible to identify a segment of the community, for example a community with a special exposure, and say that's a community need. The sample needs to represent the community in a way that is statistically appropriate.

However, involving and engaging the community is absolutely critical, and we hope to have made that clear in the RFP. It's critical to the success, and it's important to the community. There are two important ways that that needs to be approached. One is that the community needs to see that it's to their advantage to be represented in this study, and working with the community to make this happen is important.

Secondly, with additional studies, what we call adjunct studies for the community by either adding additional measures or a particular component, or an oversample in a way that can address in these ways, we expect the needs and involvement of the community to be addressed. And so, I think that answers both of those questions.

DR. BRENNER: What proportion of first time pregnancies versus previous pregnancies are expected to be enrolled at any one time during the duration of the enrollment period? Obviously, this will affect the types and sites of recruitment.

I think this is getting at first time pregnancies to somebody who is enrolled in the study, not their first pregnancy, but their first pregnancy within the study, versus subsequent pregnancies that they experience during the enrollment period. And we have done a number of analyses to look at what the expectation is for that.

Over the four- or five-year enrollment period, we expect that somewhere between 8–10 percent of the births in the study will be subsequent pregnancies, women who have already been in the study, and then become pregnant during the enrollment period, and contribute also that child to the sample.

DR. SCHEIDT: Another question, will investigators at vanguard centers have access to data and participate in analyses and data from their own site and the pooled data?

And the answer is yes, we do expect investigators at the centers to be engaged in use of, and in analyzing the data. We are more concerned that the data will be maximally used than we are with the number of people using it.

We anticipate that there be some guidelines being proposed to guide the use of data. But we expect the detailed procedures to be worked out through the steering committee. We anticipate that analyses of the primary outcomes and of the hypotheses will be carried out by the combined total of investigators participating in the study through the processes evolved in the steering committee, with assignments made through that process.

But in addition, many other analyses to be done both on the data of individual centers, and pooled data also with public use data sets, be made available in successive waves as quickly as possible.

MS. DESEAU: I want to expand on that, because another question that I have is somewhat similar. It says will investigator initiated grants be accepted which will use vanguard center-generated data, tissue, et cetera, biological samples from PIs outside of the vanguard centers?

I think it follows on from what Peter has just said. There is an anticipation that others will be able to use the data that is generated from this study. You can find a little more information on how we currently anticipate that process to be handled in the coordinating center RFP. It's Part 6. It starts on page 53. And that addresses the scientific outreach, the extant data that will be brought into the study, but the publication approaches that we anticipate.

That will help you to understand that a little bit better. But it is the hope of the study that this data will be used to its maximum advantage, and that yes, people can request use of the data in a grant process. A submitted grant proposal would go through a standard grant review process. Will that occur before the contracts awarded? Obviously, no, because the data won't be there.

In terms of the adjunct studies in particular, as opposed to a grant requesting use of the data, that is a process, the review process, exactly how we're going to set that up is not in place yet. That will be developed when we have a steering committee. But the current, if you do want to propose an adjunct study, our initial adjunct studies will come in with these proposals. They will be reviewed under the same mechanism that will be used for the complete proposal. You will notice that it's only a five point criteria.

And as Dr. Brenner has already said, we really don't expect it to be extensive at this point of the game. Just because a person is awarded a contract for a vanguard center does not mean the adjunct study is automatically awarded. But at least we have a process where we can start to consider these studies, and that will be folded into this initial review. Beyond that, we will set up a mechanism for how the reviews will be done, how they will be evaluated for the adjunct studies.

DR. BRENNER: Is there an absolute requirement that non-vanguard centers include more than one primary sampling unit? Will geographic isolation and logistical difficulties, et cetera, be taken into account in these decisions?

And the answer to that is no, at least currently it's not envisioned that there is going to be a requirement to include more than one study location. But what I want to really emphasize is that the procurement for the centers beyond the vanguard centers isn't out yet, and we have received a number of question—well, I have at the contracting office, about preparation of proposals related to non-vanguard centers. So, they want to serve as a center for one of the other

locations. And the procurement for that isn't out yet, so the details of that aren't out yet. We don't anticipate that there will be a requirement that you have to include more than one study location. And the example that is given is a good one; Honolulu would be very difficult to combine with another location. But again, the procurement for the additional locations hasn't been released, so the details aren't out yet.

And I don't know—Ginny, you have received most of these questions. Is there anything you would like to add to that?

MS. DESEAU: As we said, this is a dynamic process. And beyond these vanguard centers, we don't have the next requirement developed. We have to see how things go with the vanguard centers. We have to see if this is a realistic approach. There are a lot of questions that will be answered with this first round of contracts. So, no, we just don't know just yet.

DR. BRENNER: A couple more. Will location of offeror within the county or state be considered in the selection process, for example, in consideration of their ties to the community?

Again, anybody that is located in the Census area is considered a potential offeror for the vanguard locations. And certainly, community involvement is one of the aspects that is emphasized in this statement of work, and in the study plan. But just the mere fact that they are closer to a location doesn't necessarily mean that their proposal will be stronger in their community involvement than somebody that is located more distant.

So, the strict answer is that will location within the county or state be considered in the selection process? It's not one of the evaluation criteria. There is nothing that says that you have to be within a distance other than within the region. But community involvement certainly is one of the aspects of the proposal that will be looked at.

MS. DESEAU: And I would like to add to that. This aspect of it, there may have been some misinformation given out to people who have sent in written requests, because that wasn't completely clear to us in the contracts office at the time we started answering this deluge of questions that we got. So, Ruth's answer is the one you want to go by for now, and that will be the answer that everyone will receive from this point on.

I have another question here. It's relevant to when I was describing the review process. It's a good question. If an individual is asked to serve as a reviewer for the coordinating center or the vanguard centers, can that person be an applicant for later sites? This could give them a selective advantage.

We'll make attempts, at least for the vanguard centers, all attempts will be made to not select reviewers who are from the study locations across the country that have been already picked. We will try to be as open to potential reviewers as we can be. But on the other hand, there is no way we can know who will offer in the next round, which is a couple of years down the road.

And would they have a selective advantage? I don't think so. I think their advantage would be that they would see the difference between a good proposal and a not so good proposal. Information that is being requested under this particular solicitation may be slightly different—not slightly, we expect it will be pretty much different than what will be asked for under the study center proposals, because we are looking at a different age group, we expect there will be changes during the development of the first year or so under doing the vanguard pilot studies, et cetera.

So, from our perspective we don't think that they will have a major selective advantage. So, we'll make all attempts that we can to not choose people who are most likely to be proposing for the study centers, but there is no guarantee that one won't be participating. And the

information that they get should not be of any—they will know who has made a proposal, but that's just for the vanguard centers. We'll think about this some more, and it is a good question, but we'll make all attempts to be as fair as possible.

DR. SCHEIDT: Another quick one. If selection of sites and segments and households is so carefully based on a probabilistic model and representativeness, can you explain why the RFP calls for volunteer couples for pre-conceptual recruitment?

The volunteer refers to—well, first of all, all participants in the study are volunteers. Nobody is forced to do this, and so that's a matter of semantics. But also, volunteering is one mode of access, but only from those who are selected to be in the sample. A good example, in those counties where because of the number of births, 100 percent of the births in the counties are to be included, we expect to recruit from a household approach. But couples will be missed.

We expect to recruit from providers. Some couples may be missed. And some who are in the sample may volunteer, but they have to be in the sample. And if the center makes it known and advertises and promotes the study, then those who would be eligible to be in the study volunteer, that's what is meant by volunteer.

DR. BRENNER: In proposing a budget, what is the maximum number of live births that can be proposed by an offeror? We understand the minimum is 250.

The proposal should be based on the target of 250 live births per year over the five-year enrollment period. So, it's not a minimum or maximum, that's the target. That's the goal. Again, that means more women than 250, but the target goal for births is 250.

MS. DESEAU: Let me see if I can go through some of these budget-related questions also. They shouldn't take very long. Regarding environmental samples from employers, can we do, or can we provide monetary incentives, and need consent from participants?

On page 65 of the RFP it says you can provide monetary incentives. We are looking for creativity of the types of incentives that will be offered by the vanguard centers, and in terms of consent from participants, informed consent is necessary, as Dr. Fleischman has already mentioned, and as would be true for any human subject participant.

Local IRBs require/prefer that they include review of draft study protocol as part of the proposal. And can we budget funding for an IRB honorarium?

We have already answered that there should be a kind of an umbrella IRB, just to know that your organization has agreed to proceed with the study. There is no absolute requirement, but we prefer that. And can there be a budget? Once a contract is awarded, yes, but for preproposal costs, no. If you need to have the IRB review done before the proposal is sent in, that is considered part of your pre-proposal costs.

Guidance to estimate the amount of funding for FTEs for the budget and use the salary rate limit on page 28 of the RFP.

We are not providing a monetary guidance for how much we think labor will cost. It's part of the evaluation criteria to give us an indication of the labor mix, and the expertise within the personnel that are proposed. That's part of our evaluation, to give us an indication that there is a complete understanding of the project.

And the salary rate limit is applicable, as for all federal government contracts. There is a ceiling that it cannot be exceeded for the direct costs of people. I think right now it's $175,700, so that's pretty substantial anyhow.

But another question related to effort is the qualifications of individuals are important. Thank you, that is true. What form of CV are you requesting?

We need a full academic CV. We want to be able to evaluate the qualifications of the

personnel who are being proposed. That's certainly true for any key personnel. If it's somebody like a data entry clerk, we don't need that kind of [information], so again, this is an indication of the understanding of the project if you provide us with the appropriate qualifications of the personnel.

Allowable costs. This is kind of a more complicated question, but the answer is fairly simple. It says, as office furnishings and equipment are not allowable, and then it goes on to ask about specialized hardware and software needed to communicate, let me just answer in general.

The equipment is an allowable cost. For the vanguard centers we have already determined though that all of the IMS-related equipment will be provided by the coordinating center. Again, review the statement of work for the coordinating center to get a full understanding of this requirement.

There are a few pieces of equipment that we recognize that the vanguard centers should provide on their own, being a capable facility. And they can be purchased using contract funds, and that's a freezer, refrigerator. These things are spelled out in the RFP notes to offeror. We say assume that you will either have or need certain storage capacities.

There are some unallowable costs, and they are listed as general government requirements in Section J, and also in Part B of the acquisition. Just know that we expect the offerors to have certain facility capabilities, and the coordinating center will be providing anything that needs to be common across the organization, except for those freezers and refrigerators, and which you can budget for.

And there are a couple of questions about travel. Can cost of travel for such meetings be included for the co-PI? And another one says, travel costs prohibited or restricted, and it goes on to ask the question more specifically.

In general I can just answer you, there is an expectation that there will be travel costs generated at the vanguard centers. The number of trips that are anticipated, we have tried to provide you with our assumptions in the development of our own cost estimates for what we think this project should cost. Those are included in notes to offerors. Those are included within the contract.

Can a co-PI be included? Well, that's up to you guys. You can propose a number of travelers, but we have already told you what we assume is the required number of travelers. It doesn't mean that our assumption is the only way to go. If you can justify anything in the budget, we will look at it. It will be taken into consideration.

And if an offeror is found to be in the competitive range, negotiations will ensue, so they may come out, they may not, but there will be negotiations with all offerors in the competitive range. Let me give you a quick run down of that process, because this is different than grants, and I know a lot of you are more familiar with the grant environment.

MR. SONGCO: Hi, I'm Dave Songco. I'm the IT guy. I'm absolutely delighted that this solicitation was so clear that you didn't have a single question for me. But should one pop into your mind, you can of course submit it up to December 9 I think it was.

So, also, we were restricted. I saw a number of you I recognize as colleagues, and of course we weren't allowed to talk to you. So, I can say hello to everyone, that's fair. And I have to go, so I'll say good-bye.

MS. DESEAU: And on that note, the general process is after the solicitations are reviewed by this peer review group a determination will be made of the competitive range, which will be decided based on all of the evaluation criteria that are in Section M of the RFP, which is the technical quality, as well as the cost considerations. Negotiations will ensue with those who

are considered to be in the competitive range, and from those we will determine both in this case the number of contracts to be awarded, as well as to whom they will be awarded.

Is there a page limit on the business or technical proposals? Not in the contract environment, there is no page limit. It's always easier if it's understandable and concise, but there is no page limit.

What is approximate notice of BAFO and then award dates?

The BAFOs will probably be requested in early August or mid-August in order to make an award date in September. And as is stated in the RFP already, we anticipate an award date by September 30. It can be before that. If our negotiations are going quickly enough, you will know.

If you're in the competitive range, you will know when the BAFO will be needed, and we expect it will be during the summer time, and we're looking towards August right now. It depends on how many awards we are actually able to make. And again, funding is a prime criteria for that, besides quality of the proposals, but it also depends on the cost of the proposals that come in, how many awards we can make.

If we find it's to our benefit to make just two or three awards, that's what we will do. Or if we find that we can spread it out further, we will do that. Obviously, we are looking towards eight as a maximum.

Is there an estimation of when the selected vanguard centers would be notified whether the funding would be approved for each of the option years? There is a clause in the contract for options that says that we must inform between—it will be 60–90 days ahead of the exercise of the option.

For instance, if an option is due in September, just count back 60—90 days. We would let you know—so that's like July—we would let you know if the option will be exercised. Not much before that though. We don't always know our appropriations that far ahead of time, but during the process of the contract, in all practicality we usually know if an option is going to be exercised. But the actual notice of it will be 60–90 days before, and a contractor would know that also ahead of time.

Ruth do you have more, or Pete?

DR. SCHEIDT: I have one. Can an organization whose headquarters is not located in the same Census region as a vanguard center, but with a subsidiary in that Census region, be eligible to bid as a vanguard center? The RFP states that the organization can be with a subsidy, can be a candidate or eligible to be a center if that subsidiary is established at the time of the announcement of the RFP, or whose headquarters are established in the region.

The thinking here is that we wanted to approximate what we would see with the entire study, and that is again why we limited participation to the region. When we started to pool the sample, we anticipated that there would be clusters and voids. In fact, we looked at other national samples before we even did this to look at the potential impact of what we were going to have to deal with. And we examined carefully, and talked with even the agency heads of the agencies, do we really want to do this, and do we think this is the way should proceed? And that was explored very carefully. So, we know ahead of time that the geographic distribution of samples would place significant challenges for some centers, and some centers more than others.

And in answering that, we do strongly encourage partnerships, relationships, the use of subsidiaries where they existed if that's appropriate. And I just wanted to say we understand and anticipated these potential geographic challenges.

If there is a question about a specific instance, my suggestion, and Ginny, correct me if I'm wrong about this, but my suggestion would be to write us with the specific example. And we

can work it through, and think it through, and provide a response, and then communicate the principle guiding that response to everybody.

MS. DESEAU: And that's exactly true just in general for you to know, any specific questions that we may not have answered here, or that you sent already in writing that we haven't addressed, we will make all attempts to get back to specific questions, and to have them available for everybody, not just everyone here, but everybody, the public.

I'm sorry I wasn't clear about the travel. I have another follow-up question to the previous travel question, that there seems to be some conflicting language in the RFP. And in actuality it's not so conflicting, because there is in Part B of the RFP, there is some boilerplate language that says that travel costs are prohibited or restricted.

They are not prohibited, they are restricted. There are three areas in any federal government contract that are restricted. That's travel, equipment and consultants. All of those have negotiated ceilings. You may propose—there are allowable costs. But once they are negotiated, there is a ceiling established. That ceiling is not hard and fast.

As time goes by if there is a need to change that ceiling, to either bring it down or to raise it up, that's another negotiated point. But those three areas of costs differ from other areas of costs, because in other areas under a contract, you can shift money around as needed. For instance, if you anticipate labor to be $100,000, but you find that you need to use that money for some patient care costs, that money can be shifted around.

All of these are negotiated issues, but there are ceilings under which we are required by statute, our three areas under which ceilings are established, travel, equipment and consultant services. Again, they are negotiated.

There has been a request internally for me to expand on the Booz Allen Hamilton question when I mentioned GovWorks. This acquisition was actually awarded and reviewed by the NIH—not awarded, but it was reviewed by the NIH staff. The contractor fulfills our needs, and answers to our requirements.

But the contract was awarded under GovWorks, which is an acquisition service center under the Department of Interior. We used that mechanism of purchase, because it fit into IT as a purchase system that worked easier, faster and has been fine for our purposes. It just means that the Department of the Interior under GovWorks actually manages the contract. But the contractor answers to us, works with us. And it's just one of those mechanisms like GWACs(?) or MOBUS, things like that. It's just a mechanism that is used to facilitate quicker award of a contract.

That mechanism will not be used for the vanguard centers. So, we will be working directly together for the vanguard centers and the coordinating center.

Do you have any more, Ruth?

DR. BRENNER: The RFP does not address substantive expertise on the part of investigators such as obstetrics, statistics, epidemiology, et cetera. Will breadth of academic expertise be a criteria for selections?

And the answer to that is yes, and it is mentioned specifically in the evaluation criteria, so I will refer you to that section. It's in two of the evaluation criteria, the section on understanding project requirements, and a specific one on personnel qualifications and experience. So, it comes up in two places in the evaluation criteria.

DR. SCHEIDT: Let me expand on that just a little bit. Yes, by all means, as the RFP stipulates, we look for relevant expertise, and there are points awarded for it. But the proposal needs to reflect that expertise in the proposal as well. I think that almost goes without saying.

That being said, I wanted to just make an additional point that is related to that. I hope it

comes through that while for the reasons I mentioned we used a contract mechanism to carry out this endeavor, we are very interested and committed to capturing the investigative energies of the investigators and the expertise in the centers, and through the ways that we have discussed, through adjunct studies, through participation in the science of the project through the steering committee and the other mechanisms of the study. So, I just hope that that has come through in the proposals.

MS. DESEAU: And relevant to the adjunct studies, I do have a note here. I want you to be aware that the adjunct studies will not be evaluated regarding the IMS. The adjunct studies should not propose a separate IMS system. Everything will be handled through the centralized coordinating center, just in case that comes up in your considerations for an adjunct.

There has been another question, can you repeat the names of the project officers? No. The transcript will have them in it, and we are trying very hard to not promote the project officers at this stage of the acquisition. That's why this has been left up on the screen, the contracting office contacts.

The project officers obviously answer all of our technical questions, but they need to go through the contracts office, so that we can make sure that everybody gets the same information, unless it's very, very specific, and not substantive, and of course we'll answer questions to the best of our ability. But the technical answers will come from the project officer.

DR. SCHEIDT: The awardees will get to know them very well, won't they?

MS. DESEAU: So, let me just sum up today, unless there are more questions? Yes, there is one more question, which we will get to. I just want to make a bit of a summary of today.

Right now, at the end of today when you walk out, there is no change to the RFP. You can go forward and address those issues that you can recognize are not going to change. There are certain aspects of it that won't. But there will be a modification to the RFP. Remember, December 9 is when we want to receive the comments and suggestions so that we can—even if they weren't questions, but just comments that might be included in our revisions to any part of the RFP.

And then be sure to check Federal Business Opportunities. I'm assuming that all of you have already had access to that in order to access the full RFP, but when you did enter it, you should have registered to receive notices. Federal Business Opportunities is our primary source of communication with all of you and the rest of your colleagues.

And whenever there is a modification made, you will automatically be informed by having pre-registered on Federal Business Opportunities. So, that's our primary source. Then the National Children's Study Web site will of course also have that information, but it will link you back to Federal Business Opportunities.

The National Children's Study Web site is an invaluable source for you to understand the project, to understand the requirements, to understand the whole study. So, we encourage you to keep track of that. And as Peter has mentioned in one of this previous slides, you should sign up to get notices of changes to that also.

Comments by December 9. We anticipate the modifications to be out by December 16. And we hope to have the awards—well, the awards you already know the end dates when the proposals are due. And we would hope to have our awards by the end of this government fiscal year, which is September 30. It could be a little before, depending on how the negotiations go.

There is one more question, let's get to that.

DR. BRENNER: Will each vanguard center be expected to have all expertise such as toxic environmental expertise, behavior, asthma, injury, et cetera? Or will you look for expertise

across centers?

Certainly no one center is expected to have the expertise to cover the breadth of this study. They will be expected to have the expertise to carry out the study at their center, but we're certainly relying on the combined expertise of all the centers, along with the program office, the ICC and others involved with the study, and the centers can expect to have access to that expertise as well. And they can also use consultants. So, no, no one center is really expected to have all of the expertise that is needed for this study.

MS. DESEAU: Okay, and today is not the end of any of your questions. Again, we are available for answering questions along the way. This is a dynamic project. We all recognize that it's not set in stone, that it will change based on input from a lot of sources. But we hope we established a good direction to go, and a way to get the study accomplished.

Thank you all for coming today.

[Whereupon, the pre-proposal conference was adjourned at 12:45 p.m.]

List of Attendees

Abt Associates: Judi Mopsik
Abt Associates: Stacey FitzSimmons
Ansya Enterprises Solutions: Madhu Nair
Booz Allen Hamilton: Eugenia Guardia
Battelle: Joan Cwi
Battelle: Warren Strauss
Booz Allen Hamilton: Jamie Hui
Case Western Reserve University: Cynthia Beaner
Children's Hospital of Philadelphia: Babette Zemel
Columbia University: Virginia Rauh
Deblar & Associates: Larry King
Drexel University College of Medicine: Michelle Divito
Duke: Suzanne Pfeifer
Harvard Medical School: Matthew Gillman
Henry Ford Health System Detroit: Christine Cole Johnson
ICF: Andrea Baier
Mathematics Policy Research: Sameena Salvuca
Medical College of Wisconsin: Steven Leuther
Michigan State University: Ann Smith
Michigan State University: Nigel Paneth
Mount Sinai School of Medicine: Leonardo Trasarde
Mount Sinai School of Medicine: Mary McKay
National Academics: Rosemary Chalk
NORC: Craig Coelen
NORC: Harrison Greene
Pacific Health Research Institute: J. David Cuub
PHMC: Bob Ketterlinus
REDA International: Elham Eid Alldredge
Regional OB Consultants: Lorrie Mason
RTI International: Diane Wagener
RTI International: Jerry Rench
SAIC: Anne Irmie
SAIC: Kathleen McCormick
SAIC: Kathleen Stralka
Schneider Children's Hospital: Robert Koppel
Science Magazine: Jocelyn Kaiser
Sciences International: Herman Gibb
Scimetrika: Jean G. Orelien
Statistical and Evaluation Research: Calvin Jones
University of California, Irvine: Patrick Wadlwa
University of California, Los Angeles: Moira Inkelas
University of Chicago: Kathleen E. Parker
University of Minnesota: John Himes
University of Rochester: Thomas Fogg

University of Utah: Edward B. Clark
University of Utah: Sean D. Firth